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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,438	03/21/2007	Ajay Verma	044508-5008-US	6971

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EXAMINER	
LOVE, TREVOR M	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
02/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,438	VERMA ET AL.	
	Examiner	Art Unit	
	TREVOR M. LOVE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-15 and 18-38* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 18-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15 and 24-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/17/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 and 18-23 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups I, II, IV and V, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/25/2008.

Claims 1-5, 11-15, and 18-38 are pending. Claims 1-5 and 18-23 are withdrawn. Claims 11-15 and 24-38 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-15 and 24-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regards to claim 11, the claim was amended to remove the term “mammal” and replace it with the phrase “subject in need thereof”. While Applicant provide at least some examples in the specification which reference humans, rats, and rabbits, Applicant has failed to provide sufficient evidence that Applicant is in possession of a

method of promoting tissue neovascularization in any subject. Furthermore, Applicant has failed to define the metes and bounds of the term "subject".

With regards to claims 12-15 and 24-38, these claims are rejected as depending from independent claim 11 which fails to meet the written description requirement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-15 and 24-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teichberg (US PreGrant Publication 2006/0024284) as evidenced by Aminova et al (Pro-survival and pro-death effects of HIF-1α stabilization in a murine hippocampal cell line) and Lu et al (Hypoxia-inducible factor 1 Activation by Aerobic Glycolysis Implicates the Warburg Effect in Carcinogenesis).

Teichberg teaches a method of reducing extracellular brain glutamate levels by delivering a therapeutic amount of an active (see abstract). Said composition comprises an active agent that is taught as being oxaloacetate diethylester (see [0025]). Alternate active agents are taught as being oxaloacetate, pyruvate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate (see [0025]), this reads on **instant claims 11 and 34-38**. Teichberg teaches that the preferred subjects of said method are canines, felines, ovines, porcines, equines, bovines, and humans (see [0102]), this reads on **instant claim 12**. Said method is also taught as being useful for reducing brain glutamate levels in patients having coronary artery bypass surgery, which is a treatment for severe atherosclerosis. Furthermore, a patient having said surgery would necessarily be in need of wound healing (see claim 61), this reads on **instant claims 13-14**. Teichberg teaches that the composition can be applied topically (see [0126] and [0134]), this reads on **instant claim 15**. Teichberg also teaches that the composition can be administered rectally via enemas (see [0146]), by the nasal route via a spray

(see [0142]), orally via a capsule (see [0140]), ocularly via intraocular injection, which would encompass solutions and suspensions (see [0133] and [0144]), and subcutaneously via an injection of a pharmaceutical composition which comprises a carrier (see [0133] and 0127]), these read on **instant claims 24-26, and 27, 28, 29, 30, and 31, respectively**. Teichberg identifies that the composition can comprise lipophilic solvents or vehicles such as fatty oils when the composition is being administered parenterally (see [0144]), the scope of parenterally includes transdermal, this reads on **instant claim 32**. Teichberg identifies that in certain scenarios, for instance, in brain surgery, the composition is sometimes preferably applied topically (see [0126]). Teichberg also discloses that the composition can be administered in a plurality of administrations over several days or weeks and that a skilled artisan would be able to vary the amount in order to meet the specific needs of the scenario (see [0152] and [0153]), this reads on **instant claim 33**.

Teichberg fails to directly disclose the relationship between the glutamate concentration and HIF-1 mediated gene expression.

Aminova teaches that HIF levels are higher at reduced glutamate levels (see Aminova, figure 5c). Lu teaches that pyruvate regulates hypoxia inducible gene expression independently of hypoxia by stimulating the accumulation of HIF-1α (see Lu, abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the composition of Teichberg in amounts significant enough to induce HIF-1 mediated gene expression since Teichberg teaches a

composition for the reduction of glutamate, and Aminova teaches a relation between the concentrations of glutamate and HIF. There would be a reasonable expectation that Teichberg would use an effective amount based on figure 5c of Aminova wherein the relationship is identified.

With regards to the method of utilizing the composition being directed to promoting tissue neovascularization, it has been established that the composition is taught by Teichberg to be utilized on patient who are having coronary artery bypass surgery, which, like any major surgery, would require wound healing. Teichberg is teaches that the actives utilized in Teichberg reduce the amount of glutamate, which is useful for patients that are having surgery. Aminova teaches that as glutamate levels decrease, HIF increases. Thus, it can be inferred that patient in Teichberg whose glutamate levels are decreased shows increased HIF-1 expression because Aminova teaches that when glutamate levels are decreased, HIF increases. Further, instant claims recite neovascularization with the claimed compounds effective to induce HIF-1 levels. Hence, there would inherently be neovascularization occurring in the patient with whom the composition of Teichberg is being administered. Furthermore, since a composition can not be separated from its features, the composition as defined by the obvious combination set forth above would inherently promote tissue neovascularization.

Conclusion

No claims allowed. All claims rejected. No claims objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR M. LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611
January 30, 2009